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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/396,710	09/15/1999	AVI J. ASHKENAZI	P1101P2	7837

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EXAMINER	
KAUFMAN, CLAIRE M	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 12/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/396,710	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	Claire M. Kaufman	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *14-31* is/are allowed.

6)☒ Claim(s) *1-5, 10-13 and 32-47* is/are rejected.

7)☒ Claim(s) *6-9* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1/27/00*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment filed 9/17/03 has been entered.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

References previously cited on the IDS filed 1/27/00 which were specifically stated as unable to have been considered by the Examiner and which were subsequently submitted by Applicants have been considered. It is noted that the Examiner erroneously indicated that reference 277 had not been considered previously, when it was indicated on the 1449 that it had been.

Claim Rejections - 35 USC § 112, First Paragraph

Claims 1-5 and 10-13 remain rejected under 35 U.S.C. 112, first paragraph, for the reasons set forth in the previous Office action (mailed 3/17/03), pages 2-3.

Applicants argue that the term "Apo-2 receptor" is expressly defined in the specification such that agonist antibodies can be readily used in the claimed methods. The argument has been fully considered, but is not persuasive. As stated on page 3 of the previous Office action:

> The breadth of the claims as they relate to "Apo-2", recited only by name, is very broad since the specification includes "variants" in the definition. The term Apo-2 as defined in the specification includes naturally occurring and variant polypeptides (p. 12, lines 15-18 and p. 13, lines 13-26) . According to the specification (p. 12, lines 8-18), a variant must be a biologically active Apo-2 and have at least 80% amino acid sequence identity with SEQ ID NO:1. "Biologically active" is broadly defined as the ability to modulate (stimulate or inhibit) apoptosis (page 17, lines 29-35). Because of the low sequence identity of SEQ ID NO:1 to known related receptors, it is not predictable what other sequences an Apo-2 polypeptide could have while still being "biologically active" and distinguishable from other receptors of the TNF receptor family. The only Apo-2 polypeptide disclosed has SEQ ID NO:1, and no other naturally occurring or variant receptors are disclosed.

For these reasons and as discussed previously, the claimed methods encompass using antibodies that must bind and activate receptors with unknown sequences (*i.e.*, all those at least 80%

identical to SEQ ID NO:1) and vague functions related to apoptosis. Though the antibodies have a function required in the claims, to what protein sequence and/or structure the antibodies are binding in order to induce apoptosis is unknown and unpredictable. It is maintained that the it would require undue experimentation to practice the claimed method commensurate in scope with the claims.

New:

Claims 32-47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating cancer comprising exposing mammalian cancer cells expressing Apo-2 receptor to an effective amount of an Apo-2 agonist antibody which (a) binds to Apo-2 polypeptide consisting of the contiguous amino acid residues 1 to 411 of SEQ ID NO:1 and (b) stimulates apoptosis in at least one type of mammalian cancer cell *in vivo* or *ex vivo*, does not reasonably provide enablement for the above method wherein the cancer cells do not express Apo-2 receptor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

This method is for treating any cancer by exposing the cancer cells to an Apo-2 agonist antibody. In order for the agonist antibody to induce apoptosis in the cells, those cells must express Apo-2 receptor. Apoptosis might be induced in noncancerous cells which express Apo-2; however, one skilled in the art would not reasonably expect that event to lead to treatment of cancer in the absence of apoptosis of the cancer cells also. For these reasons, it would require undue experimentation to practice the claimed invention.

Prior Art

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The Examiner had discussed US Patent 6,342,369 in the previous Office action as not available as prior art. A correction of the Examiner's statements is needed. It was stated that "amino acids 32 and 410 are different between SEQ ID NO:2 of the patent and SEQ ID NO:1 of the instant application." This is not correct. All amino acids are identical and the amino acid

sequence appears in SEQ ID NO:1 of both the patent and instant application. It is noted that in the instant application and the patent, amino acid 410 is designated as "Xaa". This correction does not effect the inability to apply the patent as prior art.

Conclusion

New claims 14-31 are allowed.

Claims 6-9 remain objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (703) 305-5791 (changing to (571)272-0873 on 01/22/04). Dr. Kaufman can generally be reached Monday through Thursday from 8:30AM to 12:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached at (703) 308-6564 (changing to (571)272-0871 on 01/22/04).

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Official papers filed by fax should be directed to (703) 872-9306. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Claire M. Kaufman, Ph.D.

Patent Examiner, Art Unit 1646

December 8, 2003

LORRAINE SPECTOR
PRIMARY EXAMINER